


Exercise Training Alters Red Blood Cell Fatty Acid Desaturase Indices and Adipose Tissue Fatty Acid Profile in African Women with Obesity

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Objective: This study assessed the changes in red blood cell total phospholipid (RBC-TPL) and subcutaneous adipose tissue (SAT) fatty acid (FA) composition in response to 12 weeks of exercise training in South African women with obesity and the associations with changes in cardio-metabolic risk factors.

Methods: Previously sedentary women were randomized into control ($n=15$) or exercise ($n=20$) groups. RBC-TPL and SAT FA profiles, SAT gene expression, systemic inflammatory markers, liver fat, and insulin sensitivity (S_i) were measured before and after the intervention.

Results: Compared with control, exercise training induced decreases in RBC-TPL dihomo- γ -linolenic acid content and stearoyl-CoA desaturase-1 and increased delta-5 desaturase-estimated activity ($P<0.05$). In the combined group, these changes correlated with changes in circulating leptin and TNF- α ($P<0.05$), as well as lower liver fat ($P<0.01$). Exercise training decreased saturated FA (lauric and myristic acids) and increased polyunsaturated FA (eicosadienoic and adrenic acids) ($P<0.05$) in abdominal SAT, whereas γ -linolenic acid decreased ($P<0.01$) in gluteal SAT. These changes in RBC-TPL and SAT FA compositions were not associated with changes in SAT gene expression and S_i .

Conclusions: Exercise training alters RBC-TPL desaturase activities, which correlate with lower liver fat and systemic inflammation but not with the improvement of S_i .

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Introduction

Progressive lipid accumulation in obesity can lead to an impairment of adipose tissue (AT) storage capacity followed by alteration of AT function, inflammation, and increased free fatty acid (FA) release and ectopic fat deposition (1). Higher inflammation in subcutaneous AT (SAT) has been associated with partitioning excess lipids to visceral AT and liver (2). Moreover, elevated circulating free FA concentrations induce

Study Importance

What is already known?

- ▶ Progressive excess fat accumulation may lead to the impairment of subcutaneous adipose tissue (SAT) function and the increase of free fatty acid (FA) circulating concentrations, inflammation, ectopic fat deposition, and insulin resistance.
- ▶ Alterations in red blood cell total phospholipid (RBC-TPL) and adipose tissue FA metabolism in individuals with obesity are associated with insulin resistance.
- ▶ Exercise training can modify lipid and FA metabolism and improve insulin sensitivity.

What does this study add?

- ▶ This study shows that exercise reduces RBC-TPL dihomo- γ -linolenic acid and stearoyl-CoA desaturase-1 and delta-6 desaturase indices and increases the delta-5 desaturase index.
- ▶ The changes in these estimated desaturase activities correlate with lower liver fat as well as changes in circulating levels of leptin and TNF- α but not with the improvement of insulin sensitivity.
- ▶ The effect of exercise on SAT FA composition is depot specific, with more changes occurring in the abdominal SAT than the gluteal SAT.

How might these results change the direction of research?

- ▶ The relationship between obesity-associated alterations in FA composition

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systemic inflammation (3) and reduce whole-body and organ-specific insulin sensitivity (1), altogether contributing to the development of insulin resistance (IR).

Red blood cell (RBC) membranes are good indicators of individuals' dietary FA intake because of their ability to maintain membrane composition for several weeks with low diet-induced fluctuations (4). Modifications in RBC total phospholipid (RBC-TPL) FA composition have been associated with IR (4). Moreover, increases of delta-9desaturase or stearoyl-CoA desaturase-1 (SCD1) and delta-6desaturase (D6D), as well as a reduction of

and desaturase activities and metabolic risks is specific to the tissues, blood compartments, and fraction where they occur. This should be considered in future investigations of the regulation of FA metabolism in the management of metabolic diseases associated with obesity.

delta-5desaturase (D5D) in RBC (5,6) and AT (7,8), have been associated with obesity and impairment of insulin sensitivity (4). The regulation of FA metabolism in AT is depot specific, with reported differences in FA synthesis, uptake, and release between gluteal SAT (gSAT) and abdominal SAT (aSAT) (9,10). These differences might contribute to depot-specific dissimilarities in FA composition (11,12), inflammatory profiles, and associations with metabolic risks (10). Additionally, FA metabolism varies among ethnicities, partly explained by differences in lifestyle factors such as dietary intake (13). Indeed, black African women have lower saturated FA (SFA) intake and higher intake of n-6 polyunsaturated FA (PUFA) than their white counterparts, corresponding to their circulating FA composition (14,15). These differences in dietary intake between ethnicities have also been associated with differences in basal insulin sensitivity and secretion (13), suggesting ethnic specificities in the relationship between FA and markers of IR.

Lifestyle interventions such as exercise training can induce beneficial adaptations in AT and are well established to stimulate AT lipolysis, decrease lipogenesis, and improve insulin sensitivity (16-18). Exercise training has also been shown to alter adipose FA synthesis, desaturation and elongation, and FA composition of RBC membranes (11,12,19). However, data on the effects of exercise training on FA metabolism in African populations are scarce. This is particularly relevant given the reported ethnic differences in desaturase activity and capacities of long-chain PUFA synthesis driven by genetic factors (20,21). Indeed, African Americans carry the genotype associated with higher D5D activity and they are consequently more efficient in the conversion of dihomo- γ -linolenic acid (DGLA) to arachidonic acid (AA) than their white counterparts (20,21). Furthermore, despite having less visceral AT (14,22-25) and liver fat content (26), black South African (SA) women are less insulin sensitive than their white counterparts (22). This study represents a unique opportunity to investigate whether exercise-induced improvement in insulin sensitivity is associated with changes in circulating RBC and SAT FA metabolism in black women with obesity. This may help to understand the mechanisms linking FA metabolism to IR in this specific ethnic group. Therefore, we aimed to evaluate (1) the effect of exercise training, without dietary modification, on RBC-TPL and SAT FA composition and desaturase activity in previously sedentary black SA women with obesity; and (2) the associations with changes in SAT lipid metabolism, systemic inflammatory markers, liver fat, and insulin sensitivity.

Methods

Participant characteristics

The participant characteristics and detailed design of this study have been previously described (27). Briefly, sedentary women (20-35 years, BMI 30-40 kg/m²) of African ancestry (isiXhosa) were randomized into control ($n=15$) and exercise groups ($n=20$). They did not have known metabolic or inflammatory diseases (e.g., HIV, tuberculosis, active

hepatitis, rheumatoid arthritis), and they were not taking any medications, were nonsmokers, were not pregnant or lactating, and were on injectable contraception. This study was approved by the Human Research Ethics Committee of the Faculty of Health Sciences at the University of Cape Town (HREC REF 827/2016) and registered to the Pan African Clinical Trial Register (No. PACTRW201711002789113). This study was performed in accordance with the principles of the Declaration of Helsinki (1964, amended last in Fortaleza Brazil, 2013), International Council for Harmonisation Good Clinical Practice, and the laws of South Africa. All participants provided signed written informed consent before their involvement in any aspect of the study.

Study design

The exercise training intervention included 12 weeks of combined aerobic (75%-80% peak heart rate) and resistance (60%-70% peak heart rate) training, 40 to 60 minutes per session, 4 days per week, and the sessions were supervised by a trained facilitator as previously described (27). This consisted of cardiovascular exercise in the form of aerobic dance, running, skipping, and stepping performed at a moderate-vigorous intensity. Resistance exercises included the use of participants' body weight and progressed to the use of equipment. Attendance was recorded and the exercise intensity was controlled at each session by using a heart rate monitor (Polar A300, Kempele, Finland). The control group was instructed to maintain normal daily physical activity patterns, which were monitored monthly by using accelerometry (ActivPAL3c, PAL Technologies Ltd, Glasgow, UK).

Participants completed a 7-day food frequency questionnaire before and after the exercise training program for the estimation of their dietary intake. They were instructed to maintain their habitual dietary intake. No dietary recommendations were given. Energy and macronutrient intake was analyzed as previously described (28).

Body composition, body fat distribution, and liver fat

Anthropometry, whole-body composition, and body fat distribution were estimated by using dual-energy x-ray absorptiometry (Discovery-W, software version 12.7.3.7; Hologic, Bedford, Massachusetts) (29,30). Hepatic lipid content was measured by using 3-T Skyra whole-body human magnetic resonance imaging.

Cardiorespiratory fitness

Cardiorespiratory fitness was determined by measuring peak oxygen consumption (VO_{2peak}), using a walking treadmill-based (C, Quasar LE500CE; HP Cosmos, Nussdorf-Traunstein, Germany) graded exercise test with increasing gradient (2% every minute until 16%) followed by alternate increased speed (0.5 km/hour) and gradient (1%)

until volitional exhaustion. Pulmonary gas exchange was measured to calculate $\text{VO}_{2\text{peak}}$ and respiratory exchange ratio by using a metabolic gas analysis system (CPET; Cosmed, Rome, Italy).

Blood sampling and analysis

Before and following the 12-week intervention, blood samples were collected after an overnight fast and at least 48 hours after the last exercise training session for subsequent biochemical analysis. High-sensitivity C-reactive protein (immunochemiluminometric assays; IMMULITE 1000 immunoassay system, Siemens Healthcare, Midrand, South Africa), interleukin (IL)-8, monocyte chemoattractant protein 1, tumor necrosis factor- α (TNF α) (xMAP technology; Luminex, Austin, Texas), adiponectin, and leptin (enzyme-linked immunosorbent assay [ELISA] kits; EMD Millipore Corp., St Charles, Missouri) were measured in the serum. Subsequently, participants underwent a frequently sampled intravenous glucose tolerance test to measure insulin sensitivity, using Bergman's Minimal Model of glucose kinetics as previously described (27).

Determination of RBC and AT FA composition

Pairwise analysis of RBC and SAT samples was performed, including the pre- and postintervention samples of a participant in the same batch. Abdominal SAT (around the umbilicus) and gSAT (around the right upper outer quadrant) were collected by mini liposuction after 4 to 6 hours of fasting and at least 48 hours after the last exercise training session (27). Total lipids of RBC aliquots (RBC; 300 μL) and SAT (100 mg) were extracted (2:1; vol:vol; chloroform:methanol containing 0.01% butylated hydroxytoluene) by a modification of the method of Folch et al. (31,32). Thin-layer chromatography was applied to isolate the total phospholipid fraction in the RBC total lipid extract (32). RBC-TPL FA and AT total FA percentage composition was determined by gas-liquid chromatography (32). The relative percentage of an FA methyl ester (FAME) was calculated by taking the area count of a given FAME as a percentage of the total area count of all the FAMEs identified in the sample (percent, wt:wt). The mixed standard contained saturated, monounsaturated, and polyunsaturated FAME. Product to precursor FA ratios of the samples were used as a proxy to reflect enzyme activity; 18:3n-6/18:2n-6 and 20:4n-6/20:3n-6 ratios were used to estimate D6D and D5D activities, respectively (33). SCD1 activity was estimated by the ratios of 16:1n-7/16:0 and 18:1n-9/18:0 (34).

RNA extraction, reverse transcription, and quantification of gene expression

Total RNA was extracted from SAT samples by using RNeasy Lipid Tissue Mini Kit (Qiagen Ltd, Germantown, Maryland), and 1.2 μg was reverse transcribed by using High-Capacity cDNA Reverse Transcription Kit with RNase inhibitor (Applied Biosystems Foster City, California). Real-time polymerase chain reaction (PCR) was performed for each sample (triplicate) by using QuantStudio 3 Real-Time PCR System with predesigned Taqman assays from Applied Biosystems (Warrington, UK). A standard curve was constructed for each primer-probe set by using a serial dilution of complementary DNA (cDNA) pooled from all samples. The evaluated genes were selected based on the physiological pathways involved in adipogenesis (peroxisome proliferator-activated receptor gamma [*PPARG*]), lipid metabolism (lipoprotein lipase [*LPL*], diacylglycerol O-acyltransferase 2 [*DGAT2*], perilipin 1 [*PLIN1*], adipose triglyceride lipase [*ATGL*]; also known as patatin like phospholipase domain containing 2 [*PNPLA2*]), insulin signaling (insulin receptor substrate 1 [*IRS1*], glucose transporter type

4 [*GLUT4*; also known as solute carrier family 2 member 4 [*SLC2A4*]), serine/threonine-protein kinase [*SMG1*]), and inflammation (adiponectin, leptin, macrophage migration inhibitory factor [*MIF*], monocyte chemoattractant protein 1, *IL10*, toll-like receptor 4 [*TLR4*], nuclear factor- κB [*NFKB1*], and *TNF*). The expression levels of these genes were quantified in gSAT and aSAT (TaqMan gene identifications in Supporting Information Table S1) and normalized to ribosomal protein lateral stalk subunit PO as the endogenous control. The expression levels of ribosomal protein lateral stalk subunit PO were not different between the groups and depots at both time points (data not shown).

Statistical analysis

Data were summarized and presented as mean and SD or median (interquartile range, 25th-75th percentile), depending on normality of quantitative variables. Non-normally distributed variables were transformed before all analyses. Changes in the FA composition and gene expression between the groups over time were analyzed by using two-way ANOVA with repeated measures, followed by a posthoc analysis when $P < 0.1$ for interaction effect or $P < 0.05$ for time or group effects. Pearson correlations were used to evaluate the associations between the changes in RBC-TPL and SAT FA composition as well as SAT gene expression, systemic inflammatory markers, and insulin sensitivity. Analyses were performed by using Stata statistical software 13.1 (StataCorp LP, College Station, Texas), and the significance level was set at $P < 0.05$.

Results

Basic participant characteristics and dietary macronutrient intake

The participants' characteristics are presented in Supporting Information Table S2 and they have been partly published in (28,35). In brief, cardiorespiratory fitness and body composition were not different between the groups at baseline. Following exercise training, $\text{VO}_{2\text{peak}}$ (milliliters/kilograms/minute) increased in the exercise group only ($P < 0.01$). There were small but significant decreases in body weight, BMI, waist circumference, and gynoid fat (percent of total fat mass) in the exercise group ($P < 0.05$). In contrast, body weight, BMI, waist circumference, and SAT volume increased in the control group ($P < 0.05$). Liver fat showed a tendency for an interaction effect ($P = 0.069$) and tended to decrease in the exercise group ($P = 0.074$) but not in the control group ($P = 0.356$). Notably, insulin sensitivity improved in the exercise compared with control group (median of 2.04 to 2.17×10^{-4} [mU/L] $^{-1\text{min}^{-1}}$ vs. 2.01 to 1.83×10^{-4} [mU/L] $^{-1\text{min}^{-1}}$, respectively; $P < 0.05$ for interaction). No changes in circulating inflammatory markers were observed in either group.

Dietary energy and macronutrient and FA intake were not significantly different between the groups at baseline and follow-up (Supporting Information Table S3). The reported dietary fat intake of the participants at baseline contained 34% of total energy (%E) from fat, comprising 9%E from SFA, 11%E from monounsaturated fatty acid (MUFA), and 8%E from PUFA, and this did not change in response to the intervention.

Exercise training-induced changes in RBC-TPL FA composition

At baseline, RBC-TPL FA composition was not different between groups and it constituted 44% SFA, 16% MUFA, and 40% PUFA. In response to exercise training (Table 1), RBC-TPL total SFA and

individual and total MUFA did not change and they were not different between the groups. However, stearic acid (18:0) showed a tendency for a group effect ($P=0.080$), and arachidic acid (20:0) showed a tendency for a time effect ($P=0.069$) after the intervention period (Table 1). In terms of PUFA, eicosadienoic acid (20:2n-6) decreased in both groups ($P=0.002$; time effect), whereas a trend was noted for an interaction effect ($P=0.069$) for DGLA (20:3n-6) such that it decreased in the exercise group ($P=0.019$) and not in the control group ($P=0.726$). Accordingly, the estimated enzyme activity of D5D (AA/DGLA) increased in the exercise group only ($P=0.021$), while D6D (γ -linolenic acid [GLA]) and SCD1-16 activities tended to be lower in the exercise compared with the control group at postintervention ($P=0.070$ and $P=0.048$, respectively).

Changes in SAT FA composition in response to exercise training

The baseline FA composition of SAT depots was similar between the groups and the depots and consisted of 32% SFA, 42% MUFA, and 26% PUFA in aSAT and 31% SFA, 43% MUFA, and 26% PUFA in gSAT. Tables 2 and 3 present the changes in FA composition in SAT following the exercise training. Within the aSAT depot (Table 2), lauric (12:0) and myristic (14:0) acids decreased in the exercise group ($P=0.006$ and $P=0.001$, respectively) with no change in the control group ($P>0.05$). In contrast, the monounsaturated eicosenoic acid (20:1n-9) increased in the exercise group only ($P=0.003$), whereas oleic acid (18:1n-9) and total n-9 MUFA content increased in the control group ($P=0.035$ and $P=0.031$, respectively) and not in the exercise group ($P>0.05$). In terms of PUFA, eicosadienoic (20:2n-6) and adrenic (22:4n-6) acids increased in the exercise ($P=0.023$ and $P=0.018$, respectively) and not in the control group ($P>0.05$). The estimated enzyme activities (D5D, D6D, and SCD1-16 and 18) did not change in the aSAT of either group.

Within the gSAT depot (Table 3), only GLA (18:3n-6) decreased in the exercise group ($P=0.007$) and not the control group ($P>0.05$). However, total SFA increased ($P=0.046$), while palmitoleic acid (16:1n-7) and SCD1-16 decreased over the 12 weeks in the control condition ($P=0.034$ and $P=0.023$, respectively).

Effect of exercise training on SAT gene expression

The expression of genes involved in SAT adipogenesis, lipid metabolism, insulin signaling, and inflammation (Table 4) were evaluated before and after the 12-week exercise training and control conditions. *ATGL* mRNA content decreased in gSAT of both groups ($P=0.009$ in control and $P=0.024$ in exercise group) and in aSAT of the control group ($P=0.044$), whereas *GLUT4* mRNA content increased in aSAT of both groups ($P=0.047$ in control and $P=0.018$ in exercise). The remaining evaluated genes (*IRS1*, *SCL2A4*, *SMG1*, *LPL*, *PPARG*, *PLIN1*, and *DGAT2*) did not change after the exercise training intervention. Changes in inflammatory gene expression (Supporting Information Table S2) included an increase in *IL10*, *NFKB1*, and *MIF* mRNA contents in gSAT in the exercise group only, with no changes in aSAT mRNA content in response to the intervention.

Correlations between changes in FA composition and changes in metabolic parameters

The associations between the changes in individual FA and estimated enzyme activities and the variation in systemic inflammatory

markers in response to the exercise training and control conditions are presented in Figure 1. As the associations between these changes did not differ by group (no interaction), the data were combined for the exercise and control groups. The decrease in RBC-TPL DGLA content and increase in D5D activity correlated with lower circulating leptin concentrations ($r=0.445$; $P=0.006$ and $r=-0.388$; $P=0.021$, respectively). In contrast, the decrease in RBC-TPL D6D activity was associated with lower circulating TNF α concentrations ($r=0.395$; $P=0.025$). Notably, the decrease in RBC-TPL SCD1-16 correlated with lower liver fat ($r=0.439$; $P=0.009$). There were no significant associations between the changes of the individual FA or estimated enzyme activities in both SAT depots and the changes in SAT inflammatory and lipid metabolism genes (data not shown), and changes in RBC-TPL and SAT FA composition were not associated with the improvement in insulin sensitivity.

Discussion

Twelve-week combined aerobic and resistance exercise training reduced RBC-TPL SCD1-16 and D6D (tendency) and increased D5D estimated activities, along with a reduction of DGLA (20:3n-6) and improved insulin sensitivity. Although there was no significant decrease in liver fat and improvement of systemic inflammation in response to exercise training, the decrease in estimated desaturase activities was associated with lower liver fat, changes in circulating leptin, and TNF α concentrations but not with the improvement of insulin sensitivity. Within the SAT depots, exercise training reduced individual SFA (12:0 and 14:0) and increased individual PUFA (20:2n-6 and 22:4n-6) in aSAT without changes in SAT gene expression (for lipid metabolism and insulin signaling).

The reduction in RBC-TPL SCD1-16 activity was accompanied by a trend for a reduction in individual RBC-TPL SFA (18:0 and 20:0). The dietary intake of SFA and MUFA did not change in either group over the 12-week intervention period, suggesting that these changes were not mediated by dietary FA intake. SCD1 is a marker of hepatic de novo lipogenesis and it is responsible for the conversion of SFA to MUFA (36). Increased activity of SCD1 has been associated with obesity, inflammation, and IR (8). Conversely, SCD1-knockout mice are protected against the development of obesity, hypertriglyceridemia, and IR (37), and the pharmacological inhibition of SCD1 attenuates obesity-related hepatic steatosis (38). The reduction of SCD1-16 activity is, therefore, suggestive of beneficial metabolic effects of exercise training on circulating FA metabolism. Notably, the reduction of SCD1-16 activity correlated with a trend for lower liver fat content but not with the improvement of insulin sensitivity. Compared with their white counterparts, black African women have lower SCD1 activity and lower liver fat content (26) despite lower levels of insulin sensitivity (22). Hence, the lower activity of SCD1 in these women might explain their lower liver fat content as suggested by Chung et al. (26) but not the exercise-induced improvement in insulin sensitivity.

In addition to the reduction of SCD1-16, RBC-TPL DGLA and D6D decreased and RBC-TPL D5D increased, supporting our hypothesis of favorable changes in RBC-TPL FA metabolism in response to exercise training. Indeed, plasma phospholipid D6D activity and DGLA content were shown to increase in the obese state and to positively correlate with IR (39). Moreover, circulating DGLA concentrations predict metabolic risks in individuals with obesity (36). The decrease in RBC-TPL

TABLE 1 RBC-TPL fatty acid composition (percentage) at baseline and in response to 12-week exercise training intervention

Variable	Control (n = 15)		Exercise (n = 20)		P value	
	Pre	Post	Pre	Post		
Saturated fatty acids (SFA)						
14:0 (myristic acid)	0.21 (0.18-0.25)	0.24 (0.21-0.26)	0.23 (0.19-0.27)	0.25 (0.22-0.28)	0.807	0.354
16:0 (palmitic acid)	22.00 (20.45-23.21)	21.33 (20.73-22.52)	21.31 (20.35-22.36)	21.31 (20.61-22.93)	0.560	0.663
18:0 (stearic acid)	16.56 ± 0.91	16.82 ± 1.05	16.21 ± 0.75	16.11 ± 1.01	0.520	0.080
20:0 (arachidic acid)	0.34 ± 0.04	0.34 ± 0.04	0.36 ± 0.05	0.33 ± 0.04	0.069	0.747
22:0 (behenic acid)	1.33 ± 0.14	1.35 ± 0.18	1.42 ± 0.26	1.41 ± 0.18	0.897	0.219
24:0 (lignoceric acid)	3.87 ± 0.58	4.02 ± 0.55	4.11 ± 0.80	4.19 ± 0.62	0.346	0.299
Total SFA	44.33 ± 1.82	44.38 ± 1.97	44.44 ± 1.81	44.21 ± 1.54	0.820	0.951
Monounsaturated fatty acids (MUFA)						
16:1n-7 (palmitoleic acid)	0.22 (0.19-0.3)	0.26 (0.20-0.30)	0.21 (0.19-0.27)	0.22 (0.18-0.27)	0.639	0.289
18:1n-7 (cis-vaccenic acid)	1.13 (0.95-1.28)	1.06 (0.97-1.38)	1.05 (0.92-1.25)	1.11 (1.00-1.23)	0.277	0.360
18:1n-9 (oleic acid)	10.84 (10.38-11.01)	10.95 (10.49-11.44)	10.31 (10.01-11.30)	10.59 (9.97-11.62)	0.765	0.539
20:1n-9 (eicosenoic acid)	0.18 ± 0.03	0.18 ± 0.03	0.17 ± 0.02	0.18 ± 0.02	0.734	0.974
24:1n-9 (nervonic acid)	3.27 (3.13-3.50)	3.53 (3.27-3.79)	3.63 (3.30-3.77)	3.68 (3.27-4.01)	0.068	0.423
Total n-7 MUFA	1.43 ± 0.36	1.46 ± 0.41	1.30 ± 0.24	1.32 ± 0.19	0.418	0.247
Total n-9 MUFA	14.39 (13.81-14.94)	14.53 (14.17-15.31)	14.23 (13.72-14.64)	14.47 (13.67-15.17)	0.091	0.768
Total MUFA	15.57 (15.03-16.23)	15.91 (15.47-16.47)	15.44 (15.05-15.82)	15.66 (15.08-16.48)	0.036	0.542
Polyunsaturated fatty acids (PUFA)						
20:5n-3 (EPA)	0.40 (0.32-0.47)	0.4 (0.33-0.50)	0.46 (0.36-0.53)	0.41 (0.37-0.44)	0.205	0.457
22:5n-3 (DPA n-3)	1.81 (1.66-2.06)	1.83 (1.75-1.96)	2.00 (1.75-2.12)	1.9 (1.82-2.05)	0.548	0.531
22:6n-3 (DHA)	4.05 (3.78-4.56)	4.12 (3.80-4.50)	4.52 (3.98-5.07)	4.47 (4.16-4.96)	0.617	0.143
18:2n-6 (linoleic acid)	11.57 ± 1.59	11.36 ± 1.50	11.76 ± 1.55	11.57 ± 1.16	0.119	0.654
20:2n-6 (eicosadienoic acid)	0.35 ± 0.03	0.33 ± 0.04*	0.36 ± 0.05	0.34 ± 0.04*	0.002	0.651
20:3n-6 (DGLA)	1.55 ± 0.26	1.56 ± 0.25	1.54 ± 0.23	1.47 ± 0.18*	0.187	0.479
20:4n-6 (AA)	15.73 ± 0.98	15.68 ± 1.41	15.43 ± 1.29	15.66 ± 1.24	0.580	0.687
22:4n-6 (adrenic acid)	3.44 ± 0.57	3.46 ± 0.64	3.24 ± 0.63	3.36 ± 0.42	0.282	0.408
Total PUFA	39.87 (38.35-41.15)	39.35 (38.56-41.23)	39.82 (38.76-41.26)	39.58 (38.72-41.55)	0.754	0.581
Total n-6	34.31 ± 1.71	33.06 ± 1.71	32.99 ± 2.09	33.07 ± 1.57	0.709	0.782
Total n-3	6.15 (5.83-6.74)	6.29 (6.05-6.95)	6.93 (6.27-7.52)	6.93 (6.49-7.15)	0.973	0.164
Estimated enzyme activities						
D5D	10.47 ± 2.04	10.34 ± 2.13	10.32 ± 2.11**	10.86 ± 1.83**	0.239	0.057
D6D	0.136 ± 0.020	0.139 ± 0.019	0.133 ± 0.022	0.127 ± 0.017	0.667	0.086
(SCD1)-16	0.010 (0.010-0.014)	0.012 (0.010-0.014)†*	0.010 (0.010-0.013)	0.010 (0.010-0.011)†*	0.455	0.047
(SCD1)-18	0.65 (0.65-0.65)	0.66 (0.64-0.66)	0.65 (0.64-0.68)	0.66 (0.64-0.68)	0.875	0.738

Data presented as mean ± SD for normally distributed variables and median (25th-75th percentile) for skewed variables.

*P < 0.05 represents difference between groups in response to exercise training intervention.

†P < 0.05 represents difference between groups at post-training.

P < 0.1 highlighted in bold represents trends of time, group, or interaction effects within and between groups after exercise training intervention.

EPA, eicosapentaenoic acid; DPA, docosapentaenoic acid; DHA, docosahexaenoic acid; DGLA, dihomo-γ-linolenic acid; AA, arachidonic acid; D5D, delta-5-desaturase index (20:4n-6/20:3n-6); D6D, delta-6-desaturase index (18:3n-6/18:2n-6); SCD1, stearoyl-CoA desaturase-1 [SCD1-16; 16:1n-7/16:0; SCD1-18; 18:1n-9/18:0].

TABLE 2 Fatty acid composition (percentage) of abdominal subcutaneous adipose tissue at baseline and in response to 12-week exercise training intervention

Variable	Control (n=15)		Exercise (n=20)		P value		
	Pre	Post	Pre	Post	Time	Group	Interaction
Saturated fatty acids (SFA)							
12:0 (lauric acid)	0.36 (0.32-0.46)	0.40 (0.33-0.46)	0.49 (0.38-0.62)**	0.45 (0.37-0.56)**	0.251	0.085	0.019
14:0 (myristic acid)	2.79 (2.44-3.17)	2.86 (2.51-3.07)	3.08 (2.70-3.37)**	2.94 (2.64-3.25)**	0.120	0.359	0.004
16:0 (palmitic acid)	22.43±1.31	22.60±1.21	22.77±1.08	22.64±0.74	0.794	0.535	0.448
17:0 (heptadecanoic acid)	0.38 (0.35-0.44)	0.36 (0.33-0.47)	0.39 (0.35-0.44)	0.40 (0.35-0.45)	0.989	0.742	0.965
18:0 (stearic acid)	5.72±1.66	5.54±1.46	5.60±1.01	5.77±1.20	0.829	0.935	0.257
20:0 (arachidic acid)	0.15 (0.12-0.18)	0.13 (0.11-0.18)	0.14 (0.13-0.18)	0.16 (0.13-0.18)	0.706	0.583	0.306
22:0 (behenic acid)	0.05 (0.04-0.05)	0.05 (0.04-0.05)	0.04 (0.04-0.05)	0.04 (0.04-0.05)	0.706	0.932	0.186
Total SFA	31.94±3.34	31.96±2.95	32.52±1.62	32.43±1.63	0.742	0.538	0.683
Monounsaturated fatty acids (MUFA)							
16:1n-7 (palmitoleic acid)	6.11±2.13	6.00±1.91	5.64±1.34	5.48±1.44	0.248	0.361	0.709
18:1n-7 (cis-vaccenic acid)	2.79±0.57	2.84±0.55	2.72±0.35	2.84±0.40	0.182	0.756	0.691
18:1n-9 (oleic acid)	32.66 (31.74-33.06)**	32.84 (32.04-33.51)*	32.39 (32.04-32.92)	32.78 (32.05-33.70)	0.012	0.772	0.504
20:1n-9 (eicosenoic acid)	0.67±0.10	0.67±0.12	0.70±0.13	0.76±0.10**	0.059	0.135	0.033
Total n-7 MUFA	8.91±7.65	8.84±2.40	8.36±1.55	8.32±1.72	0.601	0.413	0.864
Total n-9 MUFA	33.32 (32.46-33.78)**	33.58 (32.72-34.27)**	33.07 (32.81-33.45)	33.51 (32.71-33.50)	0.006	0.645	0.664
Total MUFA	41.89±3.05	42.27±2.58	41.56±1.47	41.85±1.88	0.133	0.585	0.641
Polyunsaturated fatty acids (PUFA)							
18:3n-3 (ALA)	1.16±0.26	1.15±0.26	1.07±0.18	1.04±0.21	0.234	0.219	0.541
20:3n-3 (eicosatrienoic acid)	0.05 (0.05-0.06)	0.05 (0.05-0.05)	0.04 (0.04-0.05)	0.05 (0.04-0.05)	0.804	0.513	0.217
20:5n-3 (EPA)	0.07 (0.04-0.11)	0.07 (0.04-0.08)	0.07 (0.06-0.10)	0.08 (0.06-0.09)	0.349	0.261	0.816
22:5n-3 (DPA n-3)	0.23±0.09	0.23±0.09	0.24±0.08	0.26±0.09	0.638	0.495	0.195
22:6n-3 (DHA)	0.20±0.06	0.19±0.06	0.23±0.08	0.24±0.08	0.822	0.215	0.436
18:2n-6 (linoleic acid)	22.42±2.00	22.62±2.20	22.24±1.38	21.91±1.15	0.823	0.544	0.179
18:3n-6 (GLA)	0.17±0.03	0.16±0.03	0.16±0.03	0.15±0.02	0.053	0.024	0.826
20:2n-6 (eicosadienoic acid)	0.47 (0.36-0.57)	0.50 (0.36-0.55)	0.44 (0.41-0.52)**	0.49 (0.45-0.57)**	0.178	0.355	0.090
20:3n-6 (DGLA)	0.37±0.16	0.37±0.15	0.37±0.10	0.39±0.10	0.441	0.858	0.347
20:4n-6 (AA)	0.68±0.23	0.66±0.21	0.67±0.12	0.70±0.16	0.844	0.831	0.364
22:4n-6 (adrenic acid)	0.27±0.11	0.27±0.11	0.27±0.07**	0.30±0.08**	0.262	0.745	0.042
22:5n-6 (DPA n-6)	0.07±0.03	0.07±0.02	0.08±0.03	0.08±0.03	0.411	0.230	0.564
Total PUFA	26.17±2.45	26.28±2.73	25.92±1.46	25.71±1.53	0.868	0.628	0.526
Total n-6	24.46±2.21	24.61±2.39	24.26±1.36	24.06±1.31	0.679	0.635	0.431
Total n-3	1.71±0.37	1.67±0.41	1.66±0.29	1.65±0.36	0.448	0.706	0.741
Estimated enzyme activities							
D5D	1.92±0.44	1.89±0.37	1.90±0.40	1.84±0.37	0.600	0.890	0.802
D6D	0.016±0.006	0.016±0.007	0.017±0.005	0.018±0.004	0.416	0.709	0.283
(SCD1)-16	0.28±0.10	0.27±0.10	0.25±0.06	0.24±0.047	0.167	0.471	0.528
(SCD1)-18	5.75 (4.93-7.51)	6.34 (4.75-7.89)	5.87 (5.28-6.69)	5.78 (4.78-6.40)	0.520	0.812	0.392

Data presented as mean±SD for normally distributed variables and median (25th-75th percentile) for skewed variables. *P<0.05 and **P<0.01 represent difference between groups in response to exercise training intervention. P<0.1 highlighted in bold represents trends of time or interaction effects within and between groups after exercise training intervention. ALA, alpha-linolenic acid; LA, linoleic acid; EPA, eicosapentaenoic acid; DPA, docosapentaenoic acid; DHA, docosahexaenoic acid; GLA, gamma-linolenic acid; DGLA, dihomo-gamma-linolenic acid; AA, arachidonic acid; D5D, delta-5desaturase index (20:4n-6/20:3n-6); D6D, delta-6desaturase index (18:3n-6/18:2n-6); SCD1, stearoyl-CoA desaturase-1 (SCD1-16: 16:1n-7/16:0; SCD1-18: 18:1n-9/18:0).

TABLE 3 Fatty acid composition (percentage) of gluteal subcutaneous adipose tissue at baseline and in response to 12-week exercise training intervention

Variable	Control (n=15)		Exercise (n=20)		P value	Interaction
	Pre	Post	Pre	Post		
Saturated fatty acids (SFA)						
12:0 (lauric acid)	0.38 (0.25-0.49)	0.33 (0.26-0.48)	0.47 (0.32-0.50)	0.44 (0.32-0.61)	0.443	0.141
14:0 (myristic acid)	2.56 ± 0.84	2.69 ± 0.47	2.86 ± 0.47	2.84 ± 0.42	0.921	0.346
16:0 (palmitic acid)	21.43 ± 1.35	21.80 ± 1.22	21.95 ± 1.07	22.18 ± 0.79	0.069	0.201
17:0 (heptadecanoic acid)	0.35 (0.32-0.44)	0.36 (0.31-0.44)	0.42 (0.36-0.44)	0.39 (0.34-0.47)	0.773	0.184
18:0 (stearic acid)	4.80 ± 1.59	5.15 ± 1.50	5.31 ± 1.23	5.48 ± 1.02	0.077	0.389
20:0 (arachidic acid)	0.13 (0.10-0.18)	0.14 (0.12-0.17)	0.15 (0.12-0.19)	0.16 (0.13-0.18)	0.479	0.431
22:0 (behenic acid)	0.05 (0.04-0.07)	0.04 (0.04-0.06)	0.05 (0.04-0.07)	0.05 (0.04-0.06)	0.236	0.661
Total SFA	29.72 ± 3.55#,*	30.58 ± 2.86#,*	31.19 ± 2.22	31.55 ± 1.71	0.033	0.166
Monounsaturated fatty acids (MUFA)						
16:1n-7 (palmitoleic acid)	7.27 ± 2.30#,*	6.64 ± 2.28#,*	6.20 ± 1.84	5.91 ± 1.45	0.010	0.175
18:1n-7 (cis-vaccenic acid)	3.06 ± 0.61	3.01 ± 0.62	2.96 ± 0.41	2.88 ± 0.21	0.131	0.428
18:1n-9 (oleic acid)	32.37 (32.02-33.25)	33.38 (32.54-33.31)	32.32 (31.70-33.01)	32.70 (32.28-33.28)	0.193	0.776
20:1n-9 (eicosenoic acid)	0.69 ± 0.11	0.71 ± 0.11	0.72 ± 0.10	0.75 ± 0.11	0.098	0.324
Total n-7 MUFA	10.34 ± 2.81	9.65 ± 2.82	9.16 ± 2.18	9.79 ± 1.67	0.015	0.181
Total n-9 MUFA	33.13 (32.82-33.82)	33.27 (32.24-33.03)	33.11 (32.67-33.74)	33.50 (33.04-34.13)	0.100	0.667
Total MUFA	43.59 ± 3.12	42.92 ± 3.19	42.41 ± 2.19	42.39 ± 1.75	0.101	0.282
Polyunsaturated fatty acids (PUFA)						
18:3n-3 (ALA)	1.17 (1.00-1.37)	1.21 (0.89-1.26)	1.09 (0.94-1.25)	1.07 (0.93-1.17)	0.016	0.161
20:3n-3 (eicosatrienoic acid)	0.05 (0.04-0.05)	0.05 (0.05-0.06)	0.05 (0.04-0.06)	0.04 (0.04-0.05)	0.759	0.763
20:5n-3 (EPA)	0.08 (0.05-0.1)	0.06 (0.04-0.10)	0.09 (0.08-0.12)	0.08 (0.06-0.10)	0.090	0.089
22:5n-3 (DPA n-3)	0.26 ± 0.10	0.25 ± 0.10	0.27 ± 0.08	0.27 ± 0.08	0.308	0.705
22:6n-3 (DHA)	0.22 ± 0.08	0.21 ± 0.07	0.26 ± 0.08	0.24 ± 0.07	0.310	0.159
18:2n-6 (linoleic acid)	22.72 ± 2.08	22.56 ± 2.08	22.34 ± 1.48	22.14 ± 1.25	0.298	0.600
18:3n-6 (GLA)	0.176 ± 0.035	0.170 ± 0.039	0.171 ± 0.030**	0.157 ± 0.028**	0.012	0.355
20:2n-6 (eicosadienoic acid)	0.49 ± 0.13	0.50 ± 0.12	0.51 ± 0.10	0.51 ± 0.09	0.356	0.445
20:3n-6 (DGLA)	0.42 ± 0.16	0.43 ± 0.16	0.43 ± 0.11	0.43 ± 0.12	0.986	0.953
20:4n-6 (AA)	0.70 ± 0.21	0.71 ± 0.25	0.76 ± 0.16	0.73 ± 0.14	0.569	0.591
22:4n-6 (adrenic acid)	0.29 ± 0.12	0.30 ± 0.12	0.31 ± 0.07	0.30 ± 0.08	0.855	0.771
22:5n-6 (DPA n-6)	0.06 (0.05-0.09)	0.07 (0.05-0.09)	0.08 (0.06-0.10)	0.08 (0.06-0.10)	0.368	0.326
Total PUFA	26.68 ± 2.56	26.49 ± 2.53	26.41 ± 1.64	26.06 ± 1.45	0.074	0.690
Total n-6	24.88 ± 2.23	24.75 ± 2.25	24.64 ± 1.50	24.38 ± 1.29	0.181	0.715
Total n-3	1.80 ± 0.44	1.74 ± 0.39	1.76 ± 0.25	1.68 ± 0.29	0.053	0.661
Estimated enzyme activities						
D5D	1.73 (1.50-1.98)	1.63 (1.58-1.93)	1.77 (1.43-2.02)	1.70 (1.55-1.87)	0.275	0.668
D6D	0.019 ± 0.007	0.019 ± 0.007	0.019 ± 0.005	0.020 ± 0.005	0.856	0.807
(SCD1)-16	0.36 (0.24-0.43)#,*	0.30 (0.30-0.41)#,*	0.27 (0.23-0.34)	0.27 (0.22-0.31)	0.012	0.207
(SCD1)-18	7.12 (6.33-8.26)	6.83 (5.01-8.19)	6.21 (5.77-6.81)	6.00 (5.46-7.06)	0.074	0.235

Data presented as mean ± SD for normally distributed variables and median (25th-75th percentile) for skewed variables. *P < 0.05 and **P < 0.01 represent difference between groups in response to exercise training intervention. P < 0.1 highlighted in bold represents trends of time or group effects within and between groups after exercise training intervention. ALA, α-linolenic acid; EPA, eicosapentaenoic acid; DPA, docosapentaenoic acid; DHA, docosahexaenoic acid; GLA, γ-linolenic acid; DGLA, dihomogamma-linolenic acid; AA, arachidonic acid; D5D, delta-5-desaturase index (20:4n-6/20:3n-6); D6D, delta-6-desaturase index (18:3n-6/18:2n-6); SCD1-16, 16:1n-7/16:0; SCD1-18, 18:1n-9/18:0.

TABLE 4 Depot-specific adipose tissue gene expression before and after 12-week exercise training intervention

Variables	Control (n = 15)		Exercise (n = 20)		P value		
	Pre	Post	Pre	Post	Time	Group	Interaction
Abdominal subcutaneous adipose tissue (aSAT)							
Adipogenesis							
PPARG mRNA (AU)	0.97 ± 0.40	0.93 ± 0.40	1.11 ± 0.55	0.88 ± 0.49	0.096	0.767	0.313
Lipogenesis and lipolysis							
LPL mRNA (AU)	0.94 (0.71-1.24)	0.75 (0.61-0.89)	1.03 (0.80-1.31)	0.90 (0.58-1.16)	0.082	0.293	0.305
PLIN1 mRNA (AU)	2.04 (1.28-3.03)	1.57 (1.15-2.20)	1.73 (1.07-2.47)	1.65 (1.44-2.56)	0.302	0.756	0.297
ATGL mRNA (AU)	1.34 (0.82-1.76)	1.08 (0.84-1.37)	1.02 (0.78-1.74)	0.95 (0.59-1.15)	0.027*	0.594	0.414
DGAT2 mRNA (AU)	0.92 (0.71-1.66)	1.57 (0.84-2.20)	1.02 (0.39-2.37)	1.53 (0.94-2.97)	0.085	0.655	0.662
Insulin signaling							
Adiponectin mRNA (AU)	0.76 (0.53-0.98)	0.53 (0.49-0.66)	0.79 (0.44-1.01)	0.62 (0.42-0.78)	0.020	0.627	0.800
GLUT4 mRNA (AU)	1.18 (1.01-1.77)	1.95 (1.46-2.43)	1.39 (0.71-2.43)	2.33 (1.33-3.13)	0.003**	0.535	0.915
IRS1 mRNA (AU)	1.17 (0.93-1.86)	1.57 (0.87-1.80)	1.41 (0.96-2.10)	1.35 (1.01-1.98)	0.945	0.360	0.772
SMG1 mRNA (AU)	1.35 (1.05-1.67)	1.23 (1.02-1.73)	1.30 (0.97-1.70)	1.36 (1.06-2.08)	0.849	0.953	0.151
Gluteal subcutaneous adipose tissue (gSAT)							
Adipogenesis							
PPARG mRNA (AU)	1.15 ± 0.46	0.99 ± 0.43	1.13 ± 0.41	1.13 ± 0.46	0.325	0.403	0.471
Lipogenesis and lipolysis							
LPL mRNA (AU)	1.34 (0.83-1.45)	1.06 (0.74-1.35)	1.04 (0.80-1.34)	0.32 (0.69-1.51)	0.095	0.964	0.529
PLIN1 mRNA (AU)	1.97 (1.32-2.37)	1.60 (1.32-2.42)	1.83 (1.44-2.39)	1.81 (1.04-2.48)	0.232	0.918	0.844
ATGL mRNA (AU)	1.53 (1.04-2.35)	1.20 (0.93-1.49)	1.40 (1.05-1.70)	1.02 (0.87-1.46)	0.001**	0.542	0.577
DGAT2 mRNA (AU)	1.53 (1.13-2.23)	1.23 (0.64-2.17)	1.31 (0.84-1.92)	1.21 (0.94-1.86)	0.599	0.574	0.795
Insulin signaling							
Adiponectin mRNA (AU)	0.84 (0.50-1.10)	0.52 (0.47-0.69)	0.69 (0.58-0.82)	0.64 (0.50-0.80)	0.026*	0.530	0.166
GLUT4 mRNA (AU)	1.41 (1.19-1.76)	1.62 (0.78-2.70)	1.42 (0.92-1.98)	1.92 (1.24-2.27)	0.258	0.996	0.772
IRS1 mRNA (AU)	1.08 (0.94-1.62)	1.21 (1.02-1.73)	1.31 (0.92-1.86)	1.30 (1.07-1.78)	0.439	0.405	0.626
SMG1 mRNA (AU)	1.63 (1.14-1.83)	1.23 (1.05-1.92)	1.37 (1.11-1.63)	1.48 (1.20-1.95)	0.895	0.836	0.322

Data presented as mean ± SD for normally distributed variables and median (25th-75th percentile) for skewed variables.

* $P < 0.05$, difference pre vs. post in control group.

** $P < 0.01$, difference pre vs. post in both groups.

PPARG, peroxisome proliferator-activated receptor gamma; LPL, lipoprotein lipase; PLIN1, perilipin 1; ATGL, adipose triglyceride lipase; DGAT2, diacylglycerol O-acyltransferase 2; GLUT4, glucose transporter type 4; IRS1, insulin receptor substrate 1; SMG1, serine/threonine-protein kinase.

D6D activity and the consequent reduction in DGLA content in the present study positively correlated with changes in systemic TNF α and leptin concentrations. Reduced D6D activity may result in lower conversion rates of linolenic acid to DGLA. The decrease of DGLA could also stem from its use as a substrate for production of mild anti-inflammatory eicosanoids of the 1-series to resolve the chronic low-grade proinflammatory state observed during obesity. This long-chain FA can be metabolized by cyclooxygenases and lipoxygenases to produce 1-series prostaglandins (e.g., prostaglandin E₁) and 15-(S)-hydroxy-8,11,13-eicosatrienoic acid, capable of suppressing inflammation (40). Furthermore, the increased RBC-TPL D5D activity may also explain the reduced DGLA by increased conversion rates of DGLA to AA. However, we did not find an increase in AA, although strong associations between FA desaturase variants and increased AA content have been shown in African Americans compared with European Americans (20,21). Nonetheless, the lack of increased AA after exercise training intuitively seems advantageous, as this FA is a precursor of several potent bioactive eicosanoid products with proinflammatory properties (prostaglandins, thromboxanes, and leukotrienes) (21). Accordingly, the

increased RBC-TPL D5D activity and decreased DGLA content have been associated with lowering circulating levels of leptin, a proinflammatory cytokine and an important regulator of body fatness (41). These data, therefore, suggest a protective, anti-inflammatory action of D5D. However, further investigation is needed to validate this hypothesis, as systemic inflammation did not decrease in response to this exercise training intervention. Rather, inflammatory gene expression, mainly in gSAT, was upregulated, reflecting tissue remodeling as previously reported (35). Noteworthy, the lack of association between the changes in RBC-TPL desaturases and DGLA content and changes in insulin sensitivity following this exercise training intervention suggests that the improvement of whole-body insulin sensitivity after exercise training is not directly mediated by the changes in circulating FA metabolism.

Exercise training can alter the FA exchange rate between plasma and RBC (42), and the plasma FA composition is related to AT lipid turnover (43). To elucidate the mechanisms implicated in the alterations of RBC-TPL FA composition, we investigated the effect of exercise training on SAT FA composition and gene expression. Individual SFA (12:0 and

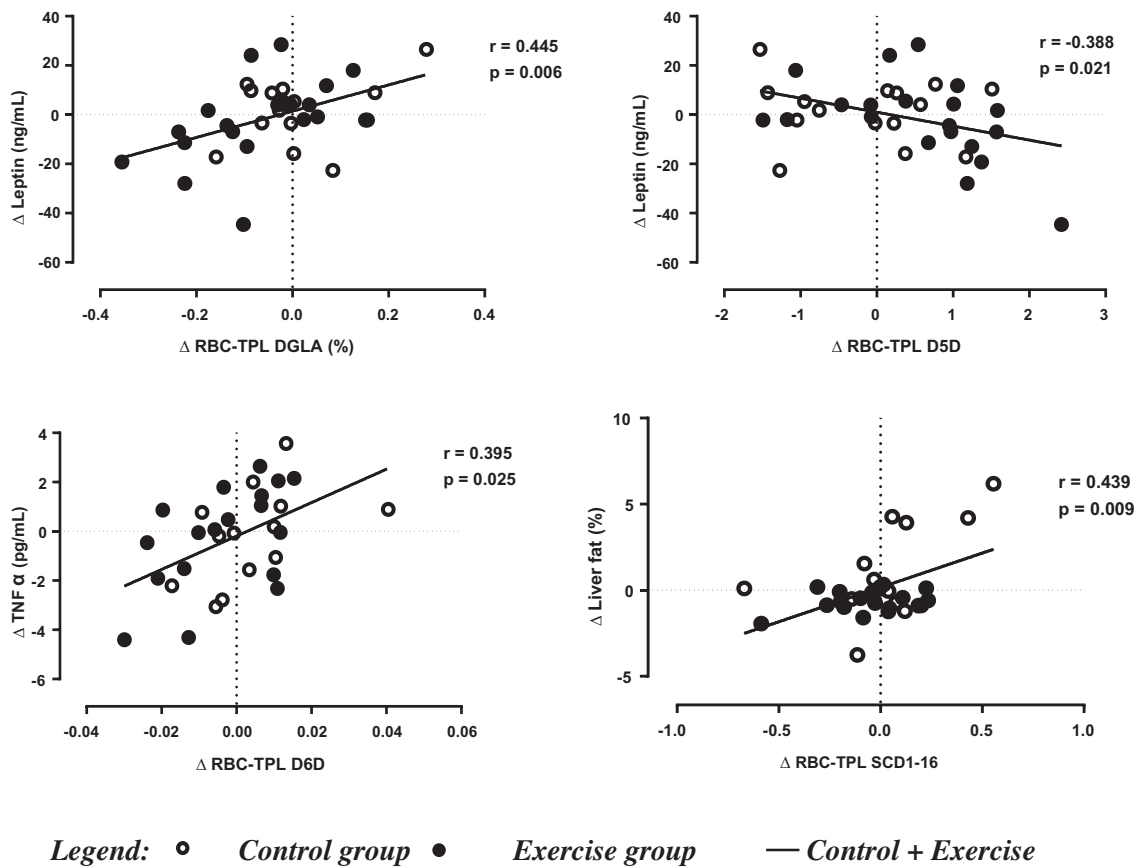


Figure 1 Correlations between changes in RBC-TPL fatty acids and estimated enzyme activities and changes of systemic inflammatory markers and liver fat in response to the exercise training intervention. Pooled data from control ($n=15$) and exercise ($n=20$) presented as changes (Δ) from pre- to postintervention. r and P values are from Pearson pairwise correlations. DGLA, dihomo- γ -linolenic acid; D5D, delta-5desaturase index (20:4n-6/20:3n6); D6D, delta-6desaturase index (18:3n-6/18:2n-6); SCD1, stearoyl-CoA desaturase-1 (SCD1-16: 16:1n-7/16:0).

14:0) decreased in aSAT after exercise training, suggesting the use of these medium-chain FA as substrates for β -oxidation. Indeed, exercise training can activate FA oxidation in adipocyte mitochondria to produce energy (11). The oxidation rate is determined by the FA chain type (saturated or unsaturated) and length, with the preferential oxidation of short to medium chains compared with long-chain FA (44). Exercise training further increased percentages of individual polyunsaturated eicosadienoic (20:2n-6) and adrenic (22:4n-6) acids in aSAT and decreased GLA (18:3n-6) in gSAT in the present study. These findings suggest an FA class- and tissue-specific effect of exercise training as previously shown in other studies (11,12). Long-chain n-6 PUFA content in the cell membrane increases the number and binding affinity of insulin receptors, whereas SFA decrease insulin binding and transport (45) and induce inflammation through NF- κ B/TLR4-related pathways (3). Therefore, we are reporting the beneficial effects of exercise training via the reduction of individual SFA and the increase of individual PUFA in aSAT. These changes in SAT FA composition were not reflective of the changes in RBC-TPL FA composition, highlighting the tissue-specific effect of exercise training. The mechanisms underlining changes in RBC-TPL FA composition after exercise training need to be further investigated.

The modifications in SAT individual FA could not be explained by changes in body fat mass, as there was no significant change in fat

mass percentage in the exercise group. This supports that the changes in SAT n-6 PUFA content are not mediated by the change in AT (12) but that they may rather reflect a direct effect of exercise training on SAT FA and lipid metabolism. However, there were no changes in the expression of genes involved in adipogenesis (*PPARG*), lipogenesis (*DGAT2*, *LPL*, *PLINI*, *GLUT4*), or lipolysis (*ATGL*), concomitantly with unaltered desaturase activities in both SAT depots after this intervention. The depot-specific changes of SAT FA composition were, therefore, unlikely because of alterations in the expression of these genes but they could relate to changes in protein expression. A longer duration of exercise training and/or higher intensity might also be required to induce more profound changes in SAT lipid metabolism (12,43). There was no significant association between the changes in SAT individual FA and insulin sensitivity. It is more likely that the reported improvement in insulin sensitivity could have derived from modifications in the skeletal muscle FA composition, which have been associated with fasting insulin concentration and insulin sensitivity in normoglycemic individuals (45); however, further research is required to address this hypothesis.

The strength of this study was the objective measurement of FA composition in the circulation (RBC) and two major depots of SAT, in combination with detailed measures of systemic inflammatory markers, SAT

gene expression, liver fat content, and insulin sensitivity. Moreover, the unique population studied and the exclusion of potential confounders such as inflammatory-related diseases and medication represent strengths of this research work. Self-reported dietary information may represent a limitation, as it may not be sensitive to potential fluctuations in dietary intake throughout the intervention and it was not sufficiently detailed for quantification of individual dietary FA composition. However, it is unlikely that this would have influenced the outcomes, as no dietary recommendations were given but rather the participants were instructed to maintain their habitual dietary intake. Another limitation was the small sample size to detect changes in liver fat and gene expression.

Conclusion

Twelve weeks of exercise training altered RBC-TPL-estimated desaturase enzyme activities by decreasing SCD1-16 and increasing D5D activity, along with a reduction of DGLA content and a trend for a reduction in D6D activity. These changes (combined groups) correlated with lower liver fat content, circulating TNF α , and leptin concentrations but not with the improvement in insulin sensitivity. Within the SAT depots, individual SFA (lauric and myristic acids) decreased, and individual n-6 PUFA (eicosadienoic and adrenic acids) increased in aSAT, but these changes were not associated with changes in SAT lipid metabolism, liver fat, or insulin sensitivity. Exercise training is associated with beneficial changes in circulating FA composition in SA women with obesity. However, the mechanisms underlying the relationship between circulating FA, desaturase activities, liver fat, and systemic inflammation, as well as the clinical relevance of the changes in SAT individual FA, requires further investigation. **O**

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